

Rapid Ethical Appraisal: A tool to design a contextualized consent process for a genetic study of podoconiosis in Ethiopia

Article (Accepted Version)

Gebresilase, Tewodros Tariku, Deresse, Zebene, Tsegay, Girmay, Tessema, Tesfaye Sisay, Aseffa, Abraham, Davey, Gail, Newport, Melanie, Tekola-Ayele, Fasil and Addissie, Adamu (2017) Rapid Ethical Appraisal: A tool to design a contextualized consent process for a genetic study of podoconiosis in Ethiopia. Wellcome Open Research, 2. 99 1-19. ISSN 2398-502X

This version is available from Sussex Research Online: <http://sro.sussex.ac.uk/id/eprint/72952/>

This document is made available in accordance with publisher policies and may differ from the published version or from the version of record. If you wish to cite this item you are advised to consult the publisher's version. Please see the URL above for details on accessing the published version.

Copyright and reuse:

Sussex Research Online is a digital repository of the research output of the University.

Copyright and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable, the material made available in SRO has been checked for eligibility before being made available.

Copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.



RESEARCH ARTICLE

Rapid Ethical Appraisal: A tool to design a contextualized consent process for a genetic study of podoconiosis in Ethiopia [version 1; referees: 3 approved with reservations]

Tewodros Tariku Gebresilase ^{1,2}, Zebene Deresse², Girmay Tsegay³,
Tesfaye Sisay Tessema ¹, Abraham Aseffa², Gail Davey ⁴, Melanie Newport ⁴,
Fasil Tekola-Ayele^{5*}, Adamu Addissie^{6*}

¹Unit of Health Biotechnology, Institute of Biotechnology, College of Natural and Computational Sciences, Addis Ababa University, Addis Ababa, Ethiopia

²Armauer Hansen Research Institute, Addis Ababa, Ethiopia

³Debre Markos University, Debre Markos, Ethiopia

⁴The Wellcome Trust Brighton and Sussex Centre for Global Health Research, Brighton and Sussex Medical School, Brighton, BN1 9PX, UK

⁵Centre for Research on Genomics and Global Health, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, 20892, USA

⁶Medical Faculty, Addis Ababa University, Addis Ababa, Ethiopia

* Equal contributors

v1 First published: 10 Oct 2017, 2:99 (doi: [10.12688/wellcomeopenres.12613.1](https://doi.org/10.12688/wellcomeopenres.12613.1))
Latest published: 10 Oct 2017, 2:99 (doi: [10.12688/wellcomeopenres.12613.1](https://doi.org/10.12688/wellcomeopenres.12613.1))

Abstract

Background: Obtaining genuine informed consent from research participants in developing countries can be difficult, partly due to poor knowledge about research process and research ethics. The situation is complicated when conducting genomic research on a disease considered familial and a reason for stigmatisation.

Methods: We used a Rapid Ethical Appraisal tool to assess local factors that were barriers to getting genuine informed consent prior to conducting a genetic study of podoconiosis (non-filarial elephantiasis) in two Zones of Ethiopia. The tool included in-depth interviews and focus group discussions with patients, healthy community members, field workers, researchers/Institutional Review Board (IRB) members, elders, religious leaders, and podoconiosis administrators who work closely with patients.

Results: Most patients and healthy community members did not differentiate research from routine clinical diagnosis. Participants felt comfortable when approached in the presence of trusted community members. Field workers and podoconiosis administrators preferred verbal consent, whereas the majority of patients and healthy community members prefer both verbal and written consent. Participants better understood genetic susceptibility concepts when analogies drawn from their day-to-day experience were used. The type of biological sample sought and gender were the two most important factors affecting the recruitment process. Most researchers and IRB members indicated that reporting incidental findings to participants is not a priority in an Ethiopian context.

Conclusions: Understanding the concerns of local people in areas where

Open Peer Review

Referee Status:

	Invited Referees		
	1	2	3
version 1			
published 10 Oct 2017	report	report	report
1	Jantina de Vries , University of Cape Town, South Africa		
	Syntia Nchangwi Munung , University of Cape Town, South Africa		
2	Angela Fenwick , University of Southampton, UK		
3	Ciara Staunton , Middlesex University, UK		
	Malcolm de Roubaix , Stellenbosch University, South Africa		

Discuss this article

Comments (0)

research is to be conducted facilitates the design of contextualized consent processes appropriate for all parties and will ultimately result in getting genuine consent.

Corresponding author: Tewodros Tariku Gebresilase (tewodrosta@gmail.com)

Author roles: Gebresilase TT: Conceptualization, Formal Analysis, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing; Deresse Z: Formal Analysis; Tsegay G: Formal Analysis, Investigation; Tessema TS: Supervision, Writing – Review & Editing; Aseffa A: Supervision, Writing – Review & Editing; Davey G: Conceptualization, Supervision, Writing – Review & Editing; Newport M: Conceptualization, Funding Acquisition, Supervision, Writing – Review & Editing; Tekola-Ayele F: Conceptualization, Investigation, Supervision, Writing – Review & Editing; Addissie A: Conceptualization, Supervision

Competing interests: No competing interests were disclosed.

How to cite this article: Gebresilase TT, Deresse Z, Tsegay G *et al.* **Rapid Ethical Appraisal: A tool to design a contextualized consent process for a genetic study of podoconiosis in Ethiopia [version 1; referees: 3 approved with reservations]** Wellcome Open Research 2017, 2:99 (doi: [10.12688/wellcomeopenres.12613.1](https://doi.org/10.12688/wellcomeopenres.12613.1))

Copyright: © 2017 Gebresilase TT *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution Licence](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The author(s) is/are employees of the US Government and therefore domestic copyright protection in USA does not apply to this work. The work may be protected under the copyright laws of other jurisdictions when used in those jurisdictions.

Grant information: This work was supported by the Wellcome Trust [100715] (Wellcome Trust Brighton and Sussex Centre for Global Health Research); the UK Medical Research Council [MR/J008621/] and from core budget of the Armauer Hansen Research Institute. *The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.*

First published: 10 Oct 2017, 2:99 (doi: [10.12688/wellcomeopenres.12613.1](https://doi.org/10.12688/wellcomeopenres.12613.1))

Introduction

Informed consent is a prerequisite for conducting ethical research on human participants. It is considered valid when participants (i) receive appropriate and comprehensive information, (ii) understand essential aspects of the research, (iii) voluntarily participate without any form of coercion, and finally (iv) agree to participate by giving either written or verbal consent.

Even though these principles are endorsed by many international and national ethics guidelines, the reality is far from this, and there is still a gap in achieving genuine informed consent, especially in studies conducted in developing countries. A meta-analysis of 21 studies conducted in Africa indicated that comprehension of key concepts (for example, randomization and placebo) differed significantly among participants, and “therapeutic misconception” is a very common issue¹. Therapeutic misconception occurs when participants do not understand the distinction between research and clinical care, and believe the purpose of their participation is to get some form of treatment rather than to generate new data. Some of the reasons for such misconceptions are high disease burden, poor access to health care, and low literacy levels in these countries¹. Another issue affecting the consent process is the extent to which a community or family interferes with the autonomous decision-making capacity of an individual. Western ethics guidelines place a huge emphasis on autonomous decision-making, and this may be contrary to the decision-making practice in most rural African settings^{2,3}.

The situation is further complicated in obtaining informed consent for genomic research due to the broad and unexpected nature of results generated from such studies. For example, in conducting sequencing and genotyping studies, researchers might discover genetic variants, which increase the risk of developing certain diseases. Such findings are medically relevant and are termed as ‘incidental findings’. In Africa, the rapid decline in sequencing cost and advances in technologies has prompted scientists to undertake genomic studies, and it is essential to develop guidelines on how to manage incidental findings in order to conduct ethical research.

In the past few years, many studies have promoted the need to contextualize the informed consent process to develop one that is ethically sound and culturally sensitive^{4,5}. One tool recently employed to explore barriers to ethical conduct of research and tailor the consent process to the local context is Rapid Ethical Appraisal (REA)^{2,3,6–8}. Similar to traditional qualitative studies, REA use in-depth interviews (IDIs), focus-group discussions (FGDs) and observation to collect data from key community informants. However, it is faster and more cost-effective in generating insights and reconciling western ethical standards with the context of developing world research settings^{6,9}.

The validity and feasibility of REA has been assessed recently in Ethiopia and was found to be relevant and acceptable in exploring social and cultural issues affecting the ethical conduct of research^{9,10}. Using this tool, for example, Tekola *et al.*, found that podoconiosis patients in Wolaita, Southern Ethiopia, were afraid to participate in a genetic study for fear that the study might

confirm the hereditary nature of the disease and fuel the existing social stigma¹¹. Studies in Cameroon also identified a number of issues regarding how to approach and obtain informed consent from participants involved in podoconiosis genetic research^{2,7}.

Even though the tool has been employed previously to explore ethical issues in Ethiopia^{3,11}, issues identified in Wolaita might not be applicable to other Ethiopian populations that differ in their social and community structure. The purpose of this REA study was therefore to explore barriers to getting genuine informed consent prior to enrolling participants in the genome-wide association study (GWAS) of podoconiosis in East Gojjam and East Wellega Zones of Ethiopia.

Methods

Ethical consideration

Ethical approval was obtained from the Armauer Hansen Research Institute (AHRI)/All Africa Leprosy and Tuberculosis Rehabilitation and Training Centre (ALERT) Ethics Review Committee, Addis Ababa, Ethiopia (registration number PO20/12) and the National Research Ethics Review Committee, Addis Ababa, Ethiopia (reference number 3.10/577/06) before conducting the study. Permission was also obtained from the Oromia and Amhara regional health bureaus. We obtained verbal consent instead of written consent as we were exploring the preferred method of consent documentation in our study area.

Study area and settings

This study was conducted from February to April 2014 in East Gojjam and East Wellega Zones (Figure 1) of North and North-Western Ethiopia, respectively, prior to enrolling participants to the podoconiosis genetic association study. This study aimed to validate the association between podoconiosis and genetic variants in the HLA region using DNA from saliva sample¹² in Wolaita, Amhara and Oromo ethnic groups in Ethiopia. Amharic and Afaan Oromo are the most widely spoken languages in East Gojjam and East Wellega (99% and 88% of the population, respectively). The majority of the population in these two Zones are subsistence farmers living in rural areas (92.28% in East Wellega and 90.08% in East Gojjam). The prevalence of podoconiosis among individuals aged 15 years and above was reported to be 3.3% in Gojjam¹³ and 2.8% in Wellega¹⁴.

Study design and participants

We conducted IDIs and FGDs with podoconiosis patients, healthy community members, podoconiosis administrators, elders/religious leaders, field workers, *kebele* (the smallest administrative unit in Ethiopia) leaders, and researcher/IRB members to explore their views on the consent process. The FGDs were comprised of single-sex adults each containing 5 to 7 individuals. Participants were chosen purposively based on their ability to discuss the issues openly and inform the phenomenon under investigation. Participants were chosen in consultation with field workers of the International Orthodox Christian Charities (Debre Markos, Gojjam) and the Ethiopian Catholic Church Clinics (Nekemte, Wellega). The field workers are experienced (>3 years of experience working in the community) and provide treatment and rehabilitation services to the communities affected by the

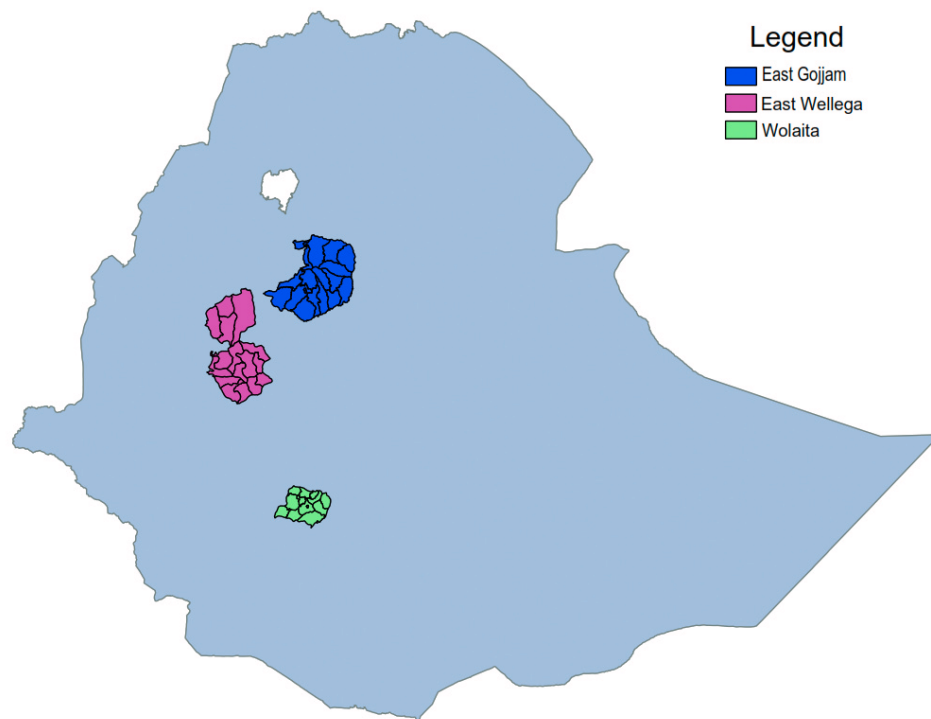


Figure 1. Map of Ethiopia showing the two study areas (East Gojjam and East Wellega). Wolaita, where the first Rapid Ethical Appraisal study was conducted, is shown for reference.

disease. Recruitment and interviewing continued until information saturation was reached and no further ideas were generated from additional interviews.

Data collection

Guide questions were prepared for each interviewee group in English ([Supplementary File 1](#)), and were then translated into Amharic and Afaan Oromo by an independent person. The interviews were back-translated by an investigator (ZA) who was not involved in conducting the interviews. With the exception of three interviews conducted in English (with podoconiosis administrators), all other interviews in East Wellega were conducted in Afaan Oromo. All the interviews in East Gojjam were conducted in Amharic. The interviews were conducted by the principal investigator (TTG) and the two co-investigators (FTA, GT), who had experience in conducting qualitative research.

Data analysis

The audio of the interviews were transcribed and translated to English by the principal investigator and two co-investigators, and checked for inconsistencies. Transcripts were imported to NVivo 10 software (QSR International) and coded independently by the PI and the co-investigators. Thematic analysis was then used to identify patterns and themes using a conceptual framework described in previous studies^{2,3,7,11}.

Results

In total, 43 IDIs and 5 FGDs were conducted ([Table 1](#)) with 31 men and 20 women from East Gojjam, and 16 men and 8 women from East Wellega. The age of respondents ranged from 18 to 68.

The issues that arose from the analysis were grouped into the following themes: perceptions towards health research and informed consent, preparation of information sheet and consent form, approaching the community, information provision, assessing comprehension, decision-making, recruitment, consent taking, and return of incidental findings.

Perceptions on health research

The majority of healthy community members and patients in the rural areas had incorrect or no understanding about research. They described research as a routine health care activity with the goal of providing treatment for their illness. Few could correctly distinguish between the two concepts.

“I believe research is a tool to maintain our health. We know our health status after participating in a research.” (Patient 9, Gojjam).

“I don’t have any idea about this [research].” (Patient 2, Wellega).

Table 1. Type and number of interviewees in each group. IDI, in-depth interviews; FGD, focus group discussion.

Participant type	East Gojjam		East Wellega	
	IDIs	FGDs	IDIs	FGDs
Patients	8	1 (n=6)	5	-
Healthy Community Members	1	3 (each n=5, 6, 7)	2	1 (n=7)
Podoconiosis administrators	2	-	3	-
Elders/religious leaders	4	-	2	-
Field Workers	3	-	3	-
Kebele Leaders	2	-	2	-
Researcher/IRB members	7 IDIs			

“Research is used to increase new knowledge, whereas diagnosis is to find the disease.” (Patient 7, Gojjam).

Some participants’ responses implied that research involving questionnaire-based data collection might be confused with aid eligibility assessment or criminal investigation.

“Nobody knows what it is, but they [the community] recognize, if new face comes with questionnaire, whether that is short or long, something will come after a while. That is their expectation.” (Podoconiosis administrator 2, Wellega).

The misconception regarding research and criminal investigation/diagnosis arise from the use of Amharic words that sound the same but have different meanings - a term referred as homophones.

“As a result of their past political and social experiences, the society differ in their understanding of words that are used to describe research, and care must be taken in this regard. For example, they may associate research with crime, police investigation and being a witness for someone.” (Podoconiosis administrator 2, Gojjam).

When asked to participate in research (in Amharic “Meremer”), some participants confused this term with another Amharic term “Mermera” which can imply either clinical diagnosis or police investigation. Moreover, research-involving drawing blood may be mistaken for screening for diseases, particularly HIV/AIDS.

“When you tell them that you are doing research, all people think it is HIV testing. It is not clear to them. They take research and diagnosis as the same.” (Elders/religious leaders 3, Gojjam).

“Research is used for identification of diseases during illness and for checking oneself (HIV-testing). People go to health facilities to get tested for HIV.” (Elders/religious leaders 1, Wellega).

Perceptions on informed consent for health research

There was unanimous agreement among all researcher/IRB members and field workers interviewed that informed consent is

a tool to communicate the study to potential participants and is essential to maintain quality of research.

“Many research participants could be vulnerable due to lack of knowledge; even educated people can sometimes be vulnerable. So, the information sheet is a tool to describe the basic of the study in an easy language.” (Researcher/IRB member 2).

“People usually give genuine answer when they are relaxed and free. They might not give you genuine answer if they are forced or coerced.” (Researcher/IRB member 6).

“Informed consent is a process of obtaining permission from our participants.” (Researcher/IRB member 1).

Preparation of consent form and information sheet

Participants stressed the need to express study information in a simple and precise manner using few technical terms.

“Some researchers don’t know what kind of information they provide. They put everything research participants do not necessarily have to know. I received 20-page information sheet and consent form when I worked as ethics secretariat. It is amazing. It shows lack of confidence” (Researcher/IRB member 4).

Patients and healthy community members wanted to be told about the objectives, implications and benefits of the study, as well as cause and prevention of podoconiosis before deciding to participate in the research. On the other hand, researcher/IRB members insisted on a need to inform prospective participants the type of study, foreseeable risks, confidentiality, voluntariness, and contact details of the principal investigator (s) and ethics committee(s) that approved the study.

“Healthy people will be volunteer if you tell them first about the cause of the disease and then what you will do to their saliva sample.” (Healthy community member 3, Gojjam).

“I want to be told about the importance of the study to my health.” (Podoconiosis patient 3, Wellega).

“Confidentiality should be secured but it is a very difficult issue since most often many people are around...You may make an effort to keep people out of the hearing distance but in a village setting it is often not easy. Then the idea of confidentiality may also be a bit different because people have most of their private things in public. Is it not?” So, I think that is the most important thing, confidentiality.” (Researcher/IRB member 3).

Some researcher/IRB members suggested doing pre-testing of the consent form and information sheet in the study site to assess its suitability and appropriateness.

“If participants are from rural areas, the information sheet and consent form have to be pretested in advance. Then we can use it if they say it is appropriate. Sometimes when I ask participants, they ask me back questions saying, ‘What do you mean by that?’ So, sometimes you can learn words or phrases from participants that you can use to describe certain information.” (Researcher/IRB member 5).

Approaching potential study participants

Many participants suggested approaching participants in the presence of known and trusted community members, including religious and *kebele* leaders, health extension workers, patient association leaders, local NGO staff. Others also mentioned using existing governmental or social structures, such as the ‘1-to-5’ networking scheme (a government-created structure where one member networks with five other people and leads the group to discuss societal issues) and *Idir* (locally established traditional self-help financial associations).

“There is a local saying ‘Yeagerun bere beageru serdo’, which is to mean ‘local problems can be best solved by the local people.’ ...They might be suspicious if you read the information to them, but they might not if someone they know reads it in front of them. You can ask the kebele administrators to read the consent form in front of them.” (Field worker 3, Gojjam).

“... They prefer to see someone whose face is not new to them.” (Podoconiosis administrator 2, Wellega).

“The health extension workers are better since it is related to health. The people may assume that they are summoned for a government meeting if they are called by the kebele administrator.” (Healthy community member 2, Gojjam).

“If you want the community at large, Kebele is better. If small group is needed, we [the church] can call them.” (Podoconiosis administrator 1, Wellega).

There was considerable discussion for and against the involvement of health extension workers (HEWs) in approaching community members for research. Most participants said that *kebele* leaders are important to confirm credibility of the study and approach prospective participants, whereas HEWs would be more appropriate to discuss health-related issues. Some participants, however, cautioned against employing HEWs because of their already-stretched work schedules.

It was indicated that the best time to approach potential participants is during the dry season, weekends (preferably Sunday) or holidays (especially religious holidays) when they are not actively engaged in farming activities.

“You can recruit many people as long as your schedule coincides with participants. You have to be very flexible. You may find a religious leader working as a farmer, so you can interview him under the shade of a tree.” (Researcher/IRB member 3).

Information provision

The local people use the Amharic term “*Zer*” or “*Zer koterio meta*” to describe hereditary diseases passed across family. Field workers and podoconiosis administrators warned that such concepts must be explained cautiously so participants do not consider podoconiosis as a hereditary disease.

“It is difficult to tell podoconiosis susceptibility concept. We do not tell them directly. If we do, they may consider susceptibility as a hereditary condition, and this may affect our work.” (Podoconiosis administrator 2, Gojjam).

“...Our target was not to put the genetic component of the disease at the centre of their attention. The community worried and think it [podoconiosis] is inherited. As I told you before, we try to give them examples and show them that they get the disease from the soil and by not wearing proper shoes...So, if somebody comes and talks about hereditary nature of podoconiosis, it counteracts our efforts. So can’t you put it in a broader sense like various ideas where this disease can come from?” (Podoconiosis administrator 3, Wellega).

Participants better understood genetic variation and difference in disease susceptibility concepts when analogies drawn from their day-to-day observations were used. In particular, many participants were familiar with the notion of improved seed yielding bigger crops, which proved to be a useful analogy. Podoconiosis administrators also mentioned that they pose a question to participants “why do some people get sick with the common cold and some do not despite living in one household?” to explain susceptibility difference in a family. They said a two-way conversation and probing is helpful to promote understanding of abstract concepts.

“...We tell them that all their family members do not develop common cold at once; some members may and some may not. So you can explain the concept of genetic susceptibility this way.” (Podoconiosis administrator 2, Gojjam).

“I don’t know how to explain this. It is difficult to me. Maybe a good explanation is needed...focusing on the nature of foot sole thickness and how the diseases go through family could also help.” (Field worker 2, Wellega).

Assessing comprehension

Field workers and podoconiosis administrators suggested to assess comprehension by asking open-ended question and said that this approach can clear any potential misconceptions about the study and enhance participants’ understanding of key study information.

“After you provide information about your study, ask them to tell you what they understood from your talk. That way you can assess their understanding level.” (Field Worker 1, Gojjam).

“Once you told them about the study in their local language, ask them open-ended questions to check if they understand what you mean.” (Podoconiosis administrator 1, Gojjam).

“After you explain the study, ask 3 or 4 participants to explain to others what you have been saying. This can help others who have misunderstood your explanation to catch-up with the group.” (Field Worker 2, Gojjam).

Decision-making, recruitment and consent taking

Most participants said that they could decide by themselves as long as they are not asked to come repeatedly, cover their own costs, stay away from their home for a long time, or are required to use family planning methods (a decision that is usually made after discussing with their partners). Some also said they reach a decision on their own if the research benefits their health – further evidence that ‘therapeutic misconception’ is common in society.

“The problem is if I am asked to pay a certain fee. So it is better if I decide together with my partner.” (Patient 2, Gojjam).

“I don’t think they will discuss with their family. The only time they do that is when they are asked to use family planning methods.” (Kebele leader 2, Gojjam).

“It depends on the decision to be made. They will definitely discuss with their family members if, for example, the treatment site is far and are asked to stay for 15 days or spend 7 days for foot massage. The whole family discuss and debate whether that person should go or not, and at the end, the idea accepted by most people win.” (Podoconiosis administrator 2, Gojjam).

Several factors that could potentially influence the recruitment process were raised and these are listed in [Table 2](#).

We found mixed views regarding the preferred form of consent documentation. Field workers and podoconiosis administrators preferred verbal consent, whereas the majority of patients and healthy community members suggested the use of both verbal and written consent to accommodate the needs of literate and illiterate participants.

“First, they have to be educated. They sign a consent form freely if they understand it well. If they are asked to sign without explanation, they may think something bad is done behind them.” (Healthy community member 4, Gojjam).

“They think something tangible if it is written and read to them. There is a local saying that” what is written on paper and what a fool once understands can never be lost or forgotten!” So, they want written information.” (Field Worker 2, Wellega).

“Healthy people might be afraid of signing; they might associate it with bad experience such as tax or confiscating their property. The situation can even be difficult with illiterates. They are suspicious and might think what is written on the document and what is read for them is different.” (Field Worker 1, Gojjam).

Return of Incidental findings

We finally asked researcher/IRB members to share their views about returning incidental findings in an Ethiopian context. Incidental findings are medically relevant information encountered in the course of a study but are beyond the aim of the study for which participants originally consented. The majority of researcher/IRB members were against disclosing incidental findings and felt that “not knowing is better than knowing”, given the poor health system in low-income countries.

“There are many severe and disabling conditions, and up to now, the health structure hasn’t been very good in addressing these. I find it unethical to tell participants they have susceptibility to rare cancer, which has no cure.” (Researcher/IRB member 6).

Table 2. Factors affecting recruitment to research.

Factors	Description
Gender	Some females (especially those that are married) might not be comfortable being interviewed alone with a stranger.
Sample type sought	Saliva is preferred over blood and other samples that require invasive collection procedures. Some associate blood sampling with HIV testing and sorcery.
Perception towards local government officials	Individuals who are not happy with local government officials may decline to participate in a research.
Previous exposure to research	Individuals with previous research exposure were not suspicious that their samples will be used in sorcery activities.
Economic status	Some people who are economically better might be offended when they are offered incentives, whereas those who are not economically strong may decline to participate for fear that they will be charged fees.

“In a country where we even don’t have enough drugs for headache, the disadvantage to know incidental finding weigh more than its advantage.” (Researcher/IRB member 5).

A few, however, said that the issue should be decided by stakeholders, including the IRB and family members. They all agreed, however, to provide participants the option whether they would like to receive their incidental finding result, but were sceptical if participants, especially those living in rural areas, understand the implications of their decision.

“I don’t think it is appropriate and ethical to reveal the result [incidental findings] unless the patient expresses their consent.” (Researcher/IRB member 4).

“The main difficulty that you will face is explaining incidental finding to participants.” (Researcher/IRB member 3).

Discussion

Obtaining genuine informed consent from participants in low-income countries can be difficult, partly due to poor knowledge about research processes and research ethics¹⁵. Cultural and social values surrounding disease and illness and familiarity with evidence-based research are among the many factors that influence the consent process¹⁶. Using REA as a tool, we identified a range of factors that can act as barriers to gaining genuine consent. We subsequently used these findings to design a contextualized consent process for a genomic study of podoconiosis (study completed; manuscript currently under preparation).

Most participants residing in rural areas did not know the distinction between research and health care and thought they were being screened to receive treatment rather than participate in research. Therapeutic misconception is common in low-income countries^{1,3,7,17,18}, especially in clinical research where providing treatment and conducting research are often carried out simultaneously¹⁹. Researchers conducting studies in such settings must assess participants’ motivations for taking part in the research. In our main genetic study, we explicitly informed participants that we were not affiliated with the local NGOs, which provide podoconiosis treatment services to the communities, and employees of the NGOs who helped us facilitate participant recruitment.

Similar to findings of Tekola *et al.*³, trusted individuals are the preferred entry point to the community. Community engagement and sensitization is critical to gain access, build trust and provide study-related information to prospective participants. For example, a religious leader spread a rumour that the vaccine used for polio immunization was contaminated with anti-fertility substances. This negatively impacted on uptake rates and resulted in discontinuation of the vaccination campaign²⁰. The campaign was later resumed after discussion with the religious leaders and convincing the population that the vaccine was safe and protects people from polio. This example highlights the influential role of community leaders and the importance of engaging them when conducting community-based studies or interventions.

Our study indicated that prospective participants need to know basic information about the study and did not require detailed information to take part in our study. Even though most information sheets and consent forms contain the purpose and objective of the study, it is important to cover all aspect of the research to help participants reach an informed decision. In the context of genomic studies, this includes information about the nature of the study, privacy, confidentiality, future use of samples and data/sample sharing plan. Participants in rural settings might not fully understand some of these concepts and a thorough explanation is needed to create awareness. In a study conducted in rural Ghana, for example, participants did not completely understand a statement about future use of stored samples, but grasped the idea when the concept was broadly explained using familiar examples, such as that “their left-over samples could be used in future studies when new ideas come up”²¹. Similarly, explaining hereditary concepts and maintaining a balance with transparency was challenging but could be done if the community’s understanding is assessed prior to conducting the study.

In our study, we explained genetic susceptibility concepts using the common cold analogy described above, saying that individuals from the same family differ in their ability to fight infections. Thus, simple and real-world examples must be used to describe abstract and scientific concepts so that participants can fully comprehend the nature of the study in which they agree to participate^{18,22}.

The field workers suggested that probing and checking the level of understanding of key study information in a question format (rather than using the traditional binary form of assessment, e.g., yes/no format) could improve comprehension. Lindegger *et al.* used 4 tools (self-report, checklist, vignettes, and narrative measures) to assess comprehension, and higher scores were recorded when checklists were used, indicating that the level of understanding is dependent on the type of tools used²³. The method suggested by the field workers needs further evaluation to check its appropriateness to the local settings. We did not implement this suggestion in our work because of resource constraints.

Participants also indicated that the language used to describe the research process could affect the consent process. For example, some may take the Amharic translation for the English word research “Mermer” to mean a police/criminal investigation. Words can have different meaning depending on the context and settings²⁴, and to avoid confusion, it is recommended to pre-test the information sheet and consent form to evaluate its appropriateness in the target population. In our case, we avoided using “Mermer” when describing research and used unambiguous words (e.g., “Tinat” for research) that reduced the possibility of negative interpretation by the community. Such an approach has been suggested by Molyneux *et al.*, who studied informed consent processes in Kenya²⁵.

Participants had misconceptions linking research with aid and expected monetary or in-kind benefits. Even though acceptable compensation is appropriate, any available benefits in resource-limited settings might result in undue influence on participants^{26,27}.

We discussed this issue with field workers and podoconiosis administrators and they suggested providing soap and other sanitary materials to promote foot hygiene, as an alternative to monetary compensation. The issue of ‘appropriate’ compensation is often controversial and context-specific, and to this end, local regulatory authorities (including ethics committees) must work with the community and researchers to establish reasonable compensation system.

Signing a consent form was found to be acceptable to patients and healthy community members and both groups supported the use of either written or verbal consent. We chose to document verbal consent for the REA study, whereas written consent was used in the main genetic study since institutional and national ethics committees in Ethiopia require written consent when conducting genetic studies on humans.

Many factors that could potentially affect participants’ recruitment were identified. Among these, gender and type of sample sought were considered by field workers and podoconiosis administrators to be the most important. In some communities, cultural practices negatively influence women’s participation in some types of research studies (e.g. sexual health issues)²⁸, and permission might be required from their husband to participate in such studies. A study conducted in Qatar, for example, indicated that a majority of Muslim female participants felt they should not be interviewed in a private room with a man and preferred the outpatient waiting area where they can be seen in public²⁹. In our genetic study, enrolment was carried out in public places (clinics, schools and *kebele* compounds) and questions that can be considered sensitive were not asked. If gender issues are anticipated, however, researchers are advised to assess the existing gender norms in their proposed study area and design culturally sensitive ways to approach potential participants (e.g., gender-matching between researchers and participants)²⁸.

All participants preferred to give saliva compared to other sample types that require invasive collection procedures (e.g., blood). Blood sampling is a very sensitive issue in most rural African settings²⁵. In a study conducted in Nigeria, for example, participants complained their blood could be used in sorcery activities³⁰. On the contrary, participants in our settings did not associate saliva with sorcery; some were even surprised that their saliva sample could be helpful for research or laboratory-based diagnosis.

In the past few years, the cost of genome sequencing has plummeted dramatically, and this has resulted in an increasing number of genomic studies. The ethical, legal and social implications (ELSI) of such studies are extensively considered in Western countries³¹, but they are not given much emphasis in Ethiopia as the medical application of genetics (e.g., genetic counselling, pharmacogenetics, etc.) is not widespread in the country. However, Ethiopian scientists are involved in national and international collaborative genomic studies (e.g., [Human Heredity and Health in Africa project](#)) and a consensus must be reached

on how to handle the ELSI issues. In our study, we particularly raised the issue of incidental findings to researcher/IRB members and the majority of them were against disclosing incidental findings arguing that there are other health issues (e.g., providing child-maternal health care) to which priority must be given. In their review, Wright *et al.*, discussed the ethical issues in conducting large-scale genomic studies in African population³², and they indicated that disclosing incidental findings is a complex issue in most countries. For example, whose duty is to inform incidental findings to research participants? Which results must be returned? Some of these issues are philosophical and active debate must continue between various stakeholders of the research enterprise to come up with a recommendation for the Ethiopian context.

Conclusions

Our study indicated that a ‘one-size fits all’ approach does not work when it comes to consent process. As described in Addissie *et al.* (2015), REA might not be required for all studies and the decision to employ the tool should be based on many factors, including the community where the study is to be conducted, the research topic, and the availability of resources⁹. However, REA is especially useful to explore issues in studies where ethical dilemmas are anticipated, including randomized clinical trials, studies conducted in research-naïve areas, and research involving sensitive topics and vulnerable groups³³. Understanding local issues will help to design contextualized consent processes appropriate for all parties and ultimately in getting genuine consent.

Data availability

The transcripts from all IDIs and FGDs are available from OSF: <http://dx.doi.org/10.17605/OSF.IO/AWKD4>³⁴. These transcripts are de-identified to maintain appropriate levels of anonymity.

Competing interests

No competing interests were disclosed.

Grant information

This work was supported by the Wellcome Trust [100715] (Wellcome Trust Brighton and Sussex Centre for Global Health Research); the UK Medical Research Council [MR/J008621/] and from core budget of the Armauer Hansen Research Institute.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Acknowledgements

We are indebted to International Orthodox Christian Charities (IOCC) staff in Debre Markos (Mr Getnet Agdew, Mr Abebe Takele, Mr Abreham Tamiru, and Sr. Tigest Getahun) for facilitating the interviews in East Gojjam. In addition, we are grateful to Mr Befirdu Mulatu (Wellega University) and Mr Megersa Arega (Ethiopian Catholic Church, Nekemte) for conducting and facilitating the interviews in East Wellega, respectively. We would also like to thank Tsegaye Hailu and Dr Kebede Deribe for providing assistance in drawing the map of the study areas.

Supplementary material

Supplementary File 1: Guide questions for the interview with different stakeholders.

[Click here to access the data.](#)

References

- Afolabi MO, Okebe JU, McGrath N, *et al.*: **Informed consent comprehension in African research settings.** *Trop Med Int Health.* 2014; **19**(6): 625–42.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Kengne-Ouafo JA, Nji TM, Tantoh WF, *et al.*: **Perceptions of consent, permission structures and approaches to the community: a rapid ethical assessment performed in North West Cameroon.** *BMC Public Health.* 2014; **14**(1): 1026.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Tekola F, Bull SJ, Farsides B, *et al.*: **Tailoring consent to context: designing an appropriate consent process for a biomedical study in a low income setting.** *PLoS Negl Trop Dis.* 2009; **3**(7): e482.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Wells RE, Kaptchuk TJ: **To tell the truth, the whole truth, may do patients harm: the problem of the nocebo effect for informed consent.** *Am J Bioeth.* 2012; **12**(3): 22–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Saidu Y, Odutola A, Jafali J, *et al.*: **Contextualizing the informed consent process in vaccine trials in developing countries.** *J Clin Res Bioeth.* 2013; **4**(1): 141.
[PubMed Abstract](#)
- Bull S, Farsides B, Tekola Ayele F: **Tailoring information provision and consent processes to research contexts: the value of rapid assessments.** *J Empir Res Hum Res Ethics.* 2012; **7**(1): 37–52.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Kengne-Ouafo JA, Millard JD, Nji TM, *et al.*: **Understanding of research, genetics and genetic research in a rapid ethical assessment in north west Cameroon.** *Int Health.* 2016; **8**(3): 197–203.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Negussie H, Addissie T, Addissie A, *et al.*: **Preparing for and Executing a Randomised Controlled Trial of Podoconiosis Treatment in Northern Ethiopia: The Utility of Rapid Ethical Assessment.** *PLoS Negl Trop Dis.* 2016; **10**(3): e0004531.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Addissie A, Davey G, Newport MJ, *et al.*: **A mixed-methods study on perceptions towards use of Rapid Ethical Assessment to improve informed consent processes for health research in a low-income setting.** *BMC Med Ethics.* 2014; **15**(1): 35.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Addissie A, Davey G, Newport M, *et al.*: **Feasibility of rapid ethical assessment for the Ethiopian health research ethics review system.** *Ethiop Med J.* 2015; **53**(Suppl 1): 25–33.
[PubMed Abstract](#)
- Tekola F, Bull S, Farsides B, *et al.*: **Impact of social stigma on the process of obtaining informed consent for genetic research on podoconiosis: a qualitative study.** *BMC Med Ethics.* 2009; **10**: 13.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Tekola Ayele F, Adeyemo A, Finan C, *et al.*: **HLA class II locus and susceptibility to podoconiosis.** *N Engl J Med.* 2012; **366**(13): 1200–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Molla YB, Tomczyk S, Amberbir T, *et al.*: **Podoconiosis in East and West Gojam Zones, northern Ethiopia.** *PLoS Negl Trop Dis.* 2012; **6**(7): e1744.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Alemu G, Tekola Ayele F, Daniel T, *et al.*: **Burden of podoconiosis in poor rural communities in Gulliso woreda, West Ethiopia.** *PLoS Negl Trop Dis.* 2011; **5**(6): e1184.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Nuffield Council on Bioethics: **The ethics of research related to healthcare in developing countries: a follow-up discussion paper follow-up Discussion Paper.** 2005.
[Reference Source](#)
- Marshall PL: **Ethical challenges in study design and informed consent for health research in resource-poor settings.** World Health Organization; 2007.
[Reference Source](#)
- Lynöe N, Hyder Z, Chowdhury M, *et al.*: **Obtaining informed consent in Bangladesh.** *N Engl J Med.* 2001; **344**(6): 460–1.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Hill Z, Tawiah-Agyemang C, Odei-Danso S, *et al.*: **Informed consent in Ghana: what do participants really understand?** *J Med Ethics.* 2008; **34**(1): 48–53.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Mfutso-Bengo J, Ndebele P, Jumbe V, *et al.*: **Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi.** *Malawi Med J.* 2008; **20**(2): 37–41.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Jegede AS: **What led to the Nigerian boycott of the polio vaccination campaign?** *PLoS Med.* 2007; **4**(3): e73.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Tindana P, Bull S, Amenga-Etego L, *et al.*: **Seeking consent to genetic and genomic research in a rural Ghanaian setting: a qualitative study of the MalariaGEN experience.** *BMC Med Ethics.* 2012; **13**: 15.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Breese PE, Burman WJ, Goldberg S, *et al.*: **Education level, primary language, and comprehension of the informed consent process.** *J Empir Res Hum Res Ethics.* 2007; **2**(4): 69–79.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Lindegger G, Milford C, Slack C, *et al.*: **Beyond the checklist: assessing understanding for HIV vaccine trial participation in South Africa.** *J Acquir Immune Defic Syndr.* 2006; **43**(5): 560–6.
[PubMed Abstract](#)
- Morgenstern J, Hegele RA, Nisker J: **Simple genetics language as source of miscommunication between genetics researchers and potential research participants in informed consent documents.** *Public Underst Sci.* 2015; **24**(6): 751–66.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Molyneux CS, Peshu N, Marsh K: **Understanding of informed consent in a low-income setting: three case studies from the Kenyan Coast.** *Soc Sci Med.* 2004; **59**(12): 2547–59.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Dawson L, Kass NE: **Views of US researchers about informed consent in international collaborative research.** *Soc Sci Med.* 2005; **61**(6): 1211–22.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Grady C: **Payment of clinical research subjects.** *J Clin Invest.* 2005; **115**(7): 1681–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Redman-MacLaren ML, Api UK, Darius M, *et al.*: **Co-interviewing across gender and culture: expanding qualitative research methods in Melanesia.** *BMC Public Health.* 2014; **14**(1): 922.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Killawi A, Khidir A, Elnashar M, *et al.*: **Procedures of recruiting, obtaining informed consent, and compensating research participants in Qatar: findings from a qualitative investigation.** *BMC Med Ethics.* 2014; **15**(1): 9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Marshall PA: **The relevance of culture for informed consent in US-funded international health research.** *Ethical and policy issues in international research: clinical trials in developing countries.* 2001; **2**: C1–C38.
- Burke W, Antommarrina AH, Bennett R, *et al.*: **Recommendations for returning genomic incidental findings? We need to talk!** *Genet Med.* 2013; **15**(11): 854–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Wright GE, Koornhof PG, Adeyemo AA, *et al.*: **Ethical and legal implications of whole genome and whole exome sequencing in African populations.** *BMC Med Ethics.* 2013; **14**(1): 21.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Addissie A: **Adoption of 'rapid ethical assessment' as a practical method for assessing ethical issues relating to biomedical research projects in Ethiopia.** University of Brighton, 2015.
[Reference Source](#)
- Gebresilase TT: **Rapid Ethical Appraisal: A Tool to Design a Contextualized Consent Process for a Genetic Study of Podoconiosis in Ethiopia.** *Open Science Framework.* 2017.
[Data Source](#)

Open Peer Review

Current Referee Status: ? ? ?

Version 1

Referee Report 07 December 2017

doi:10.21956/wellcomeopenres.13658.r28289



Ciara Staunton¹, Malcolm de Roubaix²

¹ Department of Law, Middlesex University, London, UK

² Centre for Medical Ethics and Law, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

I have the benefit of having read other reviewers' reports, and will limit my comments.

This is an interesting paper and we would like to thank you for giving us the opportunity to review this paper. Work that aims to advance the cause of informed consent in the medical research in the rural African setting is to be welcomed. We appreciate the emphasis placed on context and contextual issues like the variety of languages. Overall however, there seems to be a disconnect between the introduction, results and discussion. The abstract and introduction speaks about the genetic research, yet the results and discussion appear to focus on medical research generally. More reflection on the use of the REA and its limitations should be incorporated into this paper.

The following are specific comments on the paper.

Introduction

Genomic research raises a number of challenges for the informed consent process and it is not clear why there is a focus on incidental findings only, particularly as the results speak to a wider range of issues. A broader discussion of these issues and, in particular, in the African setting would be good.

Methods

- The conceptual framework mentioned in the data analysis should be briefly discussed.
- Would it not also have been significant to interview traditional healers as well, since many Africans have to rely on their services, they are often trusted and revered members of rural communities and their views may be influential in those societies? Should they be involved in research at all, as has been done with HIV in many settings?

Results

- Under researcher/IRB members, does this mean that they are both researchers and IRB members?
- Throughout the results, it is often not clear whether you are referring to health research generally or podoconiosis. This should be clarified.

- At times the differences between researcher/IRB and other groups are discussed, but this is not consistent e.g. perceptions on informed consent for health research contains views of IRB/researchers only. These divergent views (if any) should be included. If consistent, this should also be made clear. Furthermore, were there any variations according to location?
- Under informed consent, you refer to it as a 'tool'. Although one respondent does discuss it as a 'tool', it is a process. Moreover, in thinking of it only as a 'tool' presumably to inform', one downplays the real issue, i.e., obtaining authentic consent. Informing is just one of the ingredients of informed consent. Being a process implies something developing over time, not instantaneously.
- Had the other groups any perceptions on informed consent as they were asked about it?
- Considering the questions asked about informed consent, was there any other than it being an important process that was discussed?
- In 'decision making, recruitment and consent taking', you refer to 'most participants' and 'they'. Again, here it is important to indicate which group you are referring to, and if there are differences.
- Factors affecting recruitment to research: would females not be comfortable being interviewed by any stranger, or just a male stranger? Spelling error on 'sample type sought'.
- Previous research experience: does this mean that those with no previous exposure to research had sorcery concerns? Are some factors more important than others?
- The patient groups were not asked about incidental findings. Why is this?

Discussion

The 4th paragraph is confusing and raises a number of issues. You are stating that participants want to know basic information, but then state that information sheets and consent forms should have much more information. The discussion does not correlate with what has been stated in the results. How does this link to 'genuine' informed consent. Indeed, what is the difference between 'genuine informed consent' and 'informed consent'. The term 'authentic' informed consent may be more appropriate.

Incidental findings is a challenging topic and one that needs to be addressed in this context. Some reflection on the views expressed in these findings must be discussed. As the paper stands, the issuer regarding incidental findings is almost an afterthought, despite it appearing to be of importance in the introduction.

Research should generally benefit the society/individuals who participate. How would this society benefit? How was feedback provided to the participants, if at all?

Retention of samples/banking: This may also be an area of great concern. It is troubling that respondents may not have a clear understanding of what this means and the importance be down played, since it is 'only' buccal swabs we're dealing with. What measures should be taken to improve this misunderstanding?

Discussion on the REA, its use and limitations should be expanded.

Those 20 page hardly comprehensible consent forms are problematic in all settings, more so in this context. Discuss methods of obviating this...e.g., a shortened say 2 page summary dealing with the main issues, in plain language.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Referee Report 22 November 2017

doi:[10.21956/wellcomeopenres.13658.r26990](https://doi.org/10.21956/wellcomeopenres.13658.r26990)



Angela Fenwick

Clinical Ethics and Law, Southampton General Hospital, University of Southampton, Southampton, UK

This paper describes a study using the Rapid Ethical Appraisal (REA) method to identify potential barriers to the consent process in preparation for a following genetic study on podoconiosis. The findings are potentially interesting but the paper needs some reworking before publication.

Title: The title does not reflect the contents of the paper and I would re-phase to indicate you used REA to identify the contextual factors/issues relevant for the podoconiosis study and to reflect the conclusion in your abstract. It currently looks like you are going to discuss the method of REA rather than apply it.

Abstract:

- The first sentence of your abstract is unclear and needs clarification: whose knowledge? And what do they need to know about research ethics to consent to a study?
- In the results section you appear to confuse the process of consent with evidence of consent which is repeated later in the paper. Do you mean that some participants preferred their consent to be recorded on a written consent form? If you clarify this in the body of your text you could come back to rephrase this sentence in the abstract.
- You state that the 'type of biological sample sought and gender' were the two most important factors affecting the recruitment process' but I assume you mean the two most important factors that the participants identified for the podoconiosis study? These two are just listed in a table in your results section which seems inconsistent with the importance you attach to them.

Introduction

- This is brief and some complex issues are dealt with rather superficially; for example in relation to therapeutic misconception: might the distinction between clinical care and research be less binary in some contexts, for example participating in research may give you a diagnosis (or a risk prediction) which you could then follow up. Similarly with autonomous decision making: to what extent do people really make decisions on their own?
- I am not clear about the extent to which the use of REA is faster or cheaper than other 'tools' (which might be?) given the number of interviews and focus groups you conducted etc. Can you clarify?

Methods

- This needs expanding to include: some justification for your sample and sample size; how you decided whether to use a focus group or interview; how you dealt with these two different data sets during analysis.
- You mention the prevalence of podoconiosis for over 15yrs but you only interviewed people over 18 so you need to give an explanation of why this was the case.
- Under data analysis you say you used a conceptual framework described in previous studies and, whilst I don't think you need to go into lots of detail about this, I should not have to look up other studies to ascertain what you did. A brief summary would suffice.

Results

- In para 2 your themes should relate to your following headings more specifically. In general terms, this section would benefit from a re-organization. You move from present to past tense in this section on occasion: a general rule is that when you are reporting what participants felt, said etc you should use the past tense.
- Perceptions of health research: I am unclear whether you were asking participants about healthcare research in general or for your particular podoconiosis study: either way this needs clarifying. Without understanding this it is difficult to interpret your narrative (this is the case elsewhere also so a general clarification would help); for eg, the first quote indicates that research gives health status which may well be the case if a participant gets a diagnosis from their participation in research (as I indicated above), but this may not be the case in your particular study. (See also reference to this in the 2nd para of your discussion). The rest of this section reads rather clumsily with some repeated information and could do with streamlining.
- Perceptions on informed consent for health research: this section is rather brief given the complexity of the concept. Could it be joined with another section? Is consent a 'tool'? Isn't it a process? The 2nd quote relates to coercion and you could have highlighted this as it reflects more depth of thinking than your narrative indicates.
- Preparation of consent form and information sheet: does the first sentence relate to the forms or to the wider process of consent which includes verbal explanation? This needs clarifying up-front - and in your second para - as from the quotes I would infer it was the latter, but this doesn't match your theme heading. The quote on confidentiality in particular seems to be referring to issues inherent in the process rather than what they want included in information sheets.
- Approaching potential study participants: the title isn't clear and isn't clarified in your first sentence where 'potential' is not indicated. Are you referring to whom to approach first about a study (ie people who may not actually be the potential study participants but who act as gatekeepers/facilitators)?

- Information provision: the distinction between this theme and 'Preparation of consent form and information sheet' isn't clear to me. Are you referring here to information about podoconiosis?
- Decision making, recruitment and consent taking: there is lots wrapped up in this heading and, as I indicated above, I think your table needs an accompanying narrative if it includes the 2 factors you consider most important. The first para is confusing and needs re-writing. In relation to the para that begins: 'We found mixed views...': I don't understand why this wouldn't be under the theme, 'Preparation of consent form and information sheet'.
- Return of incidental findings: this seems a huge topic to take on in such a brief way in this paper and I would suggest considering removing it as, as it stands, does not really tell me anything useful; and I have no idea whether the podoconiosis study would involve the return of IFs from what you have written. Furthermore I am not clear why you didn't ask patient and community members questions about Ifs. If you removed this theme you could expand on gender and sample type etc., if you are short of words.

Discussion

- In the first sentence you refer to 'genuine informed consent' which is a tautology. If consent is what you outline in your first paragraph then it doesn't need additional adjectives (you use it in your abstract also). In the 4th para you say: 'it is important to cover **all** aspects of the research to help participants reach an informed decision', and 'a **thorough** explanation' is necessary but what does this mean in this context? How did your research help you understand what was appropriate?
- If you re-organise your themes and take into account the issues raised above, then your discussion will be strengthened.
- Can you say more about what you wouldn't have known for the podoconiosis study if you had just relied on previous REA studies in Ethiopia? I would like a summary of what you took forward into the podoconiosis study.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Referee Expertise: Ethical issues in genetic and genomic medicine; qualitative research methodology

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Referee Report 07 November 2017

doi:[10.21956/wellcomeopenres.13658.r26871](https://doi.org/10.21956/wellcomeopenres.13658.r26871)



Jantina de Vries  , **Syntia Nchangwi Munung** 

Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

Overall

This is an interesting paper and we thank you for giving us the opportunity to review it and provide you with some feedback that may improve the manuscript. Our most important point is to challenge you to integrate in the Discussion section some critical feedback on the limits of the REA method, or at least some reflection on whether and when REAs should be conducted if similar other REAs have already been conducted on the same diseases and/or the same scientific methodologies, albeit in different populations. Specifically, we would challenge you to consider whether the REA you report in this study yielded new information that led to the design of a 'better' (more locally attuned) consent process than would have been designed without the REA having been conducted (drawing on the results of other published REA studies conducted in Ethiopia). Early in the manuscript, you hypothesise that the linguistic and cultural variation in this part of Ethiopia justified conducting another REA – did you find that hypothesis to be true (and please give concrete examples)? And if so, what is the implication for the design of future genomic studies?

Below, we give you some feedback specifically on each of the sections of the manuscript. Some of these are mere suggestions that would enrich your discussion and description; others are more critical of the way you present your work. We hope that these suggestions are useful to you and look forward to the next iteration of this manuscript.

Introduction

- In paragraph 2 on Pg1 you refer to 'therapeutic misconception' and we would suggest that you add a reference to 'diagnostic misconception' there also. This term is now used in genomics research to describe the misconception by healthy controls that they are participating in a public screening endeavour;
- In paragraph 3 you mention one particular challenge to genomics research that has implications for the consent process – namely, incidental findings. Yet the design of genomics research harbours a number of features that impact on the consent process. In this paragraph, it would be good to reference one or two sources that outline the ways in which features of genomics research may impact on the consent process, and then also explain why in the Introduction you pick out the possibility for generating 'incidental findings' as a particular issue.
- We would suggest that the authors change their use of the term 'developing countries' to the now more commonly accepted 'Lower and Middle Income' countries or LMICs;
- You introduce the REA method as a 'recent' method (pg1) but it's not altogether recent anymore. Perhaps you could rather say 'one tool that has been applied successfully to ensure the adaptation of consent processes to local and cultural sensitivities is XYZ'.

Study design and participants:

- Add a sentence or two describing the group of “participants” referred to as Podoconiasis administrators. This is not very obvious compared to the other groups such as religious workers, researchers, IRB members;
- The FGDs were comprised of single-sex adults each containing 5 to 7 individuals. Maybe add a few sentences explaining why FGDs were composed of single-sex adults only and not otherwise.

Data Analysis

- If the PI and co-investigators are authors of the paper, it may be better to use their initials as it has been done in the other cases.
- Under ‘data collection’ – were the interviews back-translated, or were the topic guides back-translated? And if so, what was the purpose of back-translating the topic guides by an independent person? (This is of course often done for informed consent to ensure the quality of the translation, but topic guides are a different kind of material and it’s not immediately obvious that these should also be ‘back-translated’ in the same way. It would be good to explain why you did that)

Table 1

Maybe explain why there are differences in the methods used at the different sites. For example: Why were FGDs done with patients at East Gojjam and not at East Wellegam. This is important because the authors argue that even though REAs have been previously used to explore ethical issues in Ethiopia, the problems identified might not have been applicable to other Ethiopian populations that differ in social and community structure.

Results

- Overall, it may be good to get more of the researchers’ interpretation of the quotes. For example, what could explain why research participants associate health research with HIV testing and not testing for other diseases prevalent in that area?
- You describe in your results that people confused ‘research’ with police or criminal investigation, but you only offer one quote by an administrator who describes that risk exists. It is an important point though – it may impact on people’s voluntariness and ability to reject giving consent – and so merits being drawn out a bit. Have you got any quotes from prospective participants in the genomic study that illustrate this point? Could you perhaps give us a flavour of whether this was an important theme in your data or not?
- In your description of results, you sometimes describe all your interviewees as ‘participants’ and at other times you only talk about subgroups in your dataset (‘fieldworkers’ and ‘IRB members’). This is confusing, particularly when you shift focus in the article and it also only gives a very partial view of your data. E.g. when speaking about ‘understanding of research’ you talk about community members and patients, yet for ‘perceptions of IC’ you only talk about fieldworkers and IRB members – but this is not altogether clear when reading the paper. Perhaps you could talk about each stakeholder group for each of the themes you describe in the paper?
- Were Researchers/IRB members the same group of people? Where they interviewed as researchers or as IRB members or both? This needs to be stated in the method.

Perceptions on health research

- The following quote “Research is used to increase new knowledge, whereas diagnosis is to find the disease.” (Patient 7, Gojjam) does not support the observation that patients did not understand the difference between research and clinical care. Rather, it confirms that the participant knew that diagnosis as part of routine care was different from research.

- How did the perception on health research by the different groups vary and what may be the contributing factors.

Preparation of consent form and information sheet

The quote below may be moved to the next section. This is because it speaks more on approaching research participants than on the preparation of informed consent form and information sheet.

"Confidentiality should be secured but it is a very difficult issue since most often many people are around... You may make an effort to keep people out of the hearing distance but in a village setting it is often not easy. Then the idea of confidentiality may also be a bit different because people have most of their private things in public. Is it not?" So, I think that is the most important thing, confidentiality." (Researcher/IRB member 3).

Decision-making, recruitment and consent taking

The authors state that some of the "participants" also said they reached a decision on their own if the research benefits their health – further evidence that 'therapeutic misconception' is common in society. A quote from a research participant (patient) is needed to support this statement.

Discussion

- A number of claims are made in the discussion section that have not been presented in the results section. The discussion should reflect the results presented and new concepts should ideally not be introduced in the discussion. For example:
 - Most participants residing in rural areas did not know the distinction between research and health care and thought they were being screened to receive treatment rather than participate in research. Maybe first describe the two study sites, e.g. whether they are rural or urban. In the results section, provide quotes that support the claim that those in rural areas did not support the distinction between research and health care;
- In your discussion, I don't think it is appropriate to reference the Nigerian polio vaccine example to illustrate why CE is important in the context of health research – it is just one example and it's from a completely different research context & country. There are stronger ethical grounds that make CE imperative and it would be more appropriate to draw on those.
- We find the 5th paragraph of your discussion somewhat problematic. On the one hand, your data, as presented in the paper, seems to argue that participants do not want detailed information about the study but rather want information about the disease together with information about what will happen to their samples. Yet in this paragraph you argue that 'participants should really know' certain things and if they don't understand then more work should be done to explain these things better. To us, this raises two questions, namely: 1) what was really in your data, and was there perhaps a range of views that lead you to describe the kinds of information participants should have and 2) how is the list that you describe informed by your data?

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Referee Expertise: Bioethics, qualitative sociology, empirical ethics, African genomics, biobanking

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.
